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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/531,969	03/21/2000	Jan Geliebter	96700/596	6902

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EXAMINER
PARAS JR, PETER

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 07/29/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/531,969	Applicant(s) GELIEBTER ET AL.	
	Examiner Peter Paras	Art Unit 1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 May 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,9 and 37-49* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,9 and 37-49* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 9 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Applicant's amendment received on May 21, 2002 has been entered. Claim 1 has been amended. Claims 2-5 and 20 have been cancelled. Claims 1, 9, and 37-49 are pending and are under current consideration.

Terminal Disclaimer

The terminal disclaimer filed on 5/21/02 disclaiming the terminal portion of any patent granted on this application, which would extend beyond the expiration date of 6,271,211 has been reviewed and is accepted. The terminal disclaimer has been recorded.

Claim Rejections - 35 USC § 112, 1st paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 9, 37-38 and 45 as amended or originally filed are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The previous rejection is maintained for the reasons of record advanced on pages 2-4 of the Office action mailed on 2/21/02.

Applicant's arguments filed 5/21/02 have been fully considered but they are not persuasive. Applicants have argued that the specification on pages 27-28 has provided

evidence of more than thirty genes that encode potassium channels. Applicants assert that since two of these potassium channels have demonstrated effectiveness in the practice of the claimed invention, the skilled artisan would understand that potassium channels in general would likely be effective in practicing the claimed invention. See pages 2-3 of the amendment.

In response, the Examiner maintains that while the specification has described methods of causing less heightened contractility of penile and bladder smooth muscle with nucleotide sequences encoding Maxi-K and Kir6.2, the specification has not described other methods of causing less heightened contractility of smooth muscles of the urogenital tract. The Examiner further maintains that the evidence of record has not described any other nucleic acid sequences encoding potassium channels, which when introduced and expressed into smooth muscle cells of the urogenital tract cause less heightened contractility. The evidence of record has not described other nucleic acid sequences encoding potassium channels that when expressed *in vivo* can cause less heightened contractility of urogenital smooth muscle. The claimed invention as a whole is not adequately described if the claims require essential or critical elements which are not adequately described in the specification and which are not conventional in the art as of Applicant's effective filing date. Possession may be shown by reduction to practice. However, the instant specification has not reduced to practice methods of causing less heightened contractility of urogenital smooth muscle with nucleic acid sequences encoding potassium channel proteins other Maxi-k or Kir6.2 K_{ATP} subunit; such methods lack a written description. It was unknown as of Applicant's effective

filing date that any of the other nucleic acid sequences encoding potassium channel proteins embraced by the claims would have the properties of causing less heightened contractility of urogenital smooth muscle. Applicants have pointed to the specification on pages 27-28 for support of the written description of the potassium channels embraced by the claims. The specification on page 27 suggests that more than thirty K^+ channels are known to exist. The Lawson, Lawson, and Ashcroft references were cited by the specification for support of the genus of K^+ channels. These references suggest that not all K^+ channel subtypes are expressed in smooth muscle, particularly smooth muscle of the urogenital tract. Since not all K^+ channels are expressed in smooth muscle it can be argued that K^+ channels are regulated by different cell specific mechanisms. The evidence of record has not described K^+ channels from different cell types can function in smooth muscle, particularly to cause less heightened contractility of urogenital smooth muscle. Further, Applicant's specification states that despite the plethora of known K^+ channel subtypes evidence from human corporal (penile) smooth muscle suggests that only two, the K_{ATP} and Maxi-K, are physiologically relevant. See the specification on page 27 beginning at line 24 and bridging to line 2 on page 28. While Applicants have argued that two K^+ channels, K_{ATP} and Maxi-K, have shown effectiveness in practicing the claimed invention it would appear from Applicant's specification and supporting references that these are the only two K^+ channels that are relevant in the context of the claimed invention.

Accordingly, the rejection is maintained for the reasons of record and as discussed in the preceding paragraphs.

Claims 1, 9, 37-49 as originally filed or amended are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of treatment of bladder dysfunction or treatment of erectile dysfunction caused by heightened contractility of smooth muscle cells by direct injection of a nucleotide sequence encoding Maxi-K into bladder or penile smooth muscle cells, wherein expression of Maxi-K regulates smooth muscle tone by resulting in less heightened contractility of penile or bladder smooth muscle cells; and a method of treatment of erectile dysfunction caused by heightened contractility of smooth muscle cells by direct injection of a nucleotide sequence encoding the Kir6.2 K_{ATP} subunit into penile smooth muscle cells, wherein expression of Kir6.2 regulates smooth muscle tone by resulting in less heightened contractility of penile smooth muscle cells, does not reasonably provide enablement for all other methods of causing less heightened contractility in urogenital smooth muscle. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. Aspects of the previous rejection are maintained for the reasons of record advanced on pages 4-7 of the Office action mailed on 2/21/02.

The aspect of the previous enablement rejection directed to gene delivery and cell targeting is withdrawn in view of Applicant's amendments to the claims, which now require direct introduction of DNA sequences.

Applicant's arguments filed 5/21/02 have been fully considered but they are not persuasive. Applicants have asserted that the instant claims are enabled for any potassium channel protein. Applicants have based their assertions on the fact that the claimed invention works with two separate potassium channel protein in two separate urogenital smooth muscles. Applicants argue that in light of such there is no reason to believe that any other gene encoding a potassium channel protein could not substitute for the maxi-K gene or the K_{ATP} gene. Applicants submit that the skilled artisan would understand these results suggest that there is a reasonable likelihood of success in using any potassium channel gene when practicing the claimed invention. Applicants have also argued that such results suggest that gene therapy with respect to potassium channels in urogenital smooth muscle is sufficiently predictable. See pages 3-5 of the amendment.

In response, the Examiner maintains that the instant claims are not enabled for their full scope, particularly with regard to nucleic acid sequences encoding potassium channel proteins, types of urogenital smooth muscle, and effect of expression of nucleic acid sequences encoding potassium channel proteins. As set forth in the Office action mailed on 2/21/02 on pages 5-6, the working examples provided by the instant specification are only directed to the use of nucleic acid sequences encoding maxi-K or Kir6.2 for regulation of smooth muscle cells of the bladder or penis resulting in less heightened contractility. The art of gene therapy at the time the claimed invention was filed was unpredictable with respect to expression of a heterologous nucleic acid sequence and a resulting therapeutic effect (see Eck and Wilson). The evidence of

record does not provide any guidance, which exemplifies that any gene encoding any potassium channel protein can cause less heightened contractility of any urogenital smooth muscle cells. The evidence of record actually teaches away from Applicant's assertions that any potassium channel can cause less heightened contractility of any urogenital smooth muscle cell. The specification on page 27 suggests that more than thirty K^+ channels are known to exist. The Lawson, Lawson, and Ashcroft references were cited by the specification for support of the genus of K^+ channels. These references suggest that not all K^+ channel subtypes are expressed in smooth muscle, particularly smooth muscle of the urogenital tract. Since not all K^+ channels are expressed in smooth muscle it can be argued that K^+ channels are regulated by different cell specific mechanisms. The evidence of record has not provided any guidance or teaching that suggests that K^+ channels from different cell types can function in smooth muscle, particularly to cause less heightened contractility of urogenital smooth muscle. Further, Applicant's specification states that despite the plethora of known K^+ channel subtypes evidence from human corporal (penile) smooth muscle suggests that only two, the K_{ATP} and Maxi-K, are physiologically relevant. See the specification on page 27 beginning at line 24 and bridging to line 2 on page 28. While Applicants have argued that two K^+ channels, K_{ATP} and Maxi-K, have shown effectiveness in practicing the claimed invention it would appear from Applicant's specification and supporting references that these are the only two K^+ channels that are relevant in the context of the claimed invention.

It is also of interest to note that the claims as written are directed to causing less heightened contractility of urogenital smooth muscle cells in a subject. The claims may be properly interpreted to read on causing less heightened contractility of urogenital smooth muscle cells in a normal subject as the claims do not require that the subject have a particular dysfunction associated with heightened contractility of urogenital smooth muscle. The instant specification has not provided any guidance for causing less heightened contractility of urogenital smooth muscle cells in a normal subject. It is unclear and unsupported by the instant specification why the skilled artisan would cause less heightened contractility in the urogenital smooth muscle of a normal subject.

Accordingly, the rejection is maintained for the reasons of record and as discussed in the preceding paragraph.

Applicant's amendments to the claims have necessitated the following new grounds of rejection under 35 U.S.C. 112, first paragraph:

New Matter

Claims 1, 9, and 37-49 as amended or originally filed are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. 37 CFR 1.118 (a) states that "No amendment shall introduce new matter into the disclosure of an application after the filing date of the application".

The claims are directed to methods of **causing less heightened contractility of a smooth muscle in a urogenital tract of a subject** comprising the direct introduction and expression of a DNA sequence encoding a potassium channel protein in a sufficient number of **smooth muscle cells of the urogenital tract of the subject to result in less heightened contractility of the smooth muscle in the urogenital tract of the subject**.

The specification provides no implicit or explicit support for the context of less heightened contractility of a smooth muscle in a urogenital tract of a subject (the subject is interpreted to embrace a normal subject) encompassed by the bolded clauses. The specification also has not provided implicit or explicit support for generic smooth muscle of the urogenital tract. The specification has only provided support for expression of the DNA construct in the context of the claimed transgenic mouse. Applicants are reminded that it is their burden to show where the specification supports any amendments to the claims. See 37 CFR 1.121 (b)(2)(iii), the MPEP 714.02, 3rd paragraph, last sentence and also the MPEP 2163.07, last sentence.

MPEP 2163.06 notes "If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph - written description requirement. *In re Rasmussen*, 650 F.2d 1212, 211 USPQ 323 (CCPA 1981)." MPEP 2163.02 teaches that "Whenever the issue arises, the fundamental factual inquiry is whether a claim defines an invention that is clearly conveyed to those skilled in the art at the time the application was filed...If a claim is amended to include subject matter, limitations, or terminology not present in the application as filed, involving a departure from, addition

to, or deletion from the disclosure of the application as filed, the examiner should conclude that the claimed subject matter is not described in that application. MPEP 2163.06 further notes "When an amendment is filed in reply to an objection or rejection based on 35 U.S.C. 112, first paragraph, a study of the entire application is often necessary to determine whether or not "new matter" is involved. *Applicant should therefore specifically point out the support for any amendments made to the disclosure.*

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

The previous double patenting rejection over US 6,271,211 is withdrawn as Applicants have filed a proper terminal disclaimer over the patent.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner(s) should be directed to Peter Paras, Jr., whose telephone number is 703-308-8340. The examiner can normally be reached Monday-Friday from 8:30 to 4:30 (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached at 703-305-4051. Papers related to this application may be submitted by facsimile transmission. Papers should be faxed via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center numbers are (703) 308-4242 and (703) 305-3014.

Inquiries of a general nature or relating to the status of the application should be directed to Patsy Zimmerman whose telephone number is (703) 308-0009.

Peter Paras, Jr.

Art Unit 1632

Scott D. Priebe

SCOTT D. PRIEBE, PH.D
PRIMARY EXAMINER